

## Continuous Ambulatory Peritoneal Dialysis in a Patient with Human Immunodeficiency Virus Infection

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We report the case of a female patient with human immunodeficiency virus (HIV) receiving highly active antiretroviral therapy (HAART) who developed end-stage renal failure requiring continuous ambulatory peritoneal dialysis (CAPD). She experienced polymicrobial CAPD-associated peritonitis and died about 1 month after initiation of CAPD. Although CAPD is an effective dialytic therapy, infection remains its Achilles' heel. The potential risk of HIV transmission by peritoneal dialysis effluent should be noted. HAART dose should be adjusted according to renal function to minimize adverse drug effects. [*Hong Kong J Nephrol* 2004; 6(1):52–5]

**Key words:** continuous ambulatory peritoneal dialysis, CAPD, end-stage renal failure, HIV

本個案報告為一位感染人類免疫缺乏病毒 (HIV) 的女性病人，於高活性抗反轉錄病毒治療 (HAART) 期間發生末期腎衰竭，並接受連續可活動性腹膜透析 (CAPD)。在 CAPD 開始後 1 個月，她死於因 CAPD 併發之感染性腹膜炎。即使 CAPD 屬於行之有效的透析療法，但卻有導致感染性疾病之虞。此外，腹膜透析亦可能透過排放液造成 HIV 之傳播。在進行 HAART 期間，應密切注意劑量的調整，以降低不良作用對病人的影響。

### CASE REPORT

A 67-year-old lady had had a history of hypertension since 1980, but she did not seek regular medical advice. In May 2001, she tested positive for anti-human immunodeficiency virus (HIV) after her husband was diagnosed with acquired immunodeficiency syndrome (AIDS). At the same time, she was found to have impaired renal function, with a serum creatinine level of 230  $\mu$ M. Autoimmune markers, including antinuclear factor and anti-neutrophil cytoplasmic antibody, were negative. Ultrasound kidney examination revealed multiple simple cysts together with evidence of chronic parenchymal disease in both kidneys. Renal biopsy was not performed in view of the chronic nature of the disease. Anti-hypertensive therapy was adjusted for better blood pressure control.

The patient had had localized herpes zoster infection in September 2001 and *Escherichia coli* septicemia sec-

ondary to urinary tract infection requiring hospitalization in November 2001. In view of the drop in CD4 lymphocyte count to 261 cells/ $\mu$ L associated with an increase in viral RNA load to  $164 \times 1,000$  copies/mL in February 2003, highly active antiretroviral therapy (HAART) consisting of didanosine, lamivudine and nevirapine was started. The patient's renal function progressively deteriorated and reached end-stage renal failure (ESRF) in June 2003, with a serum creatinine level of 800  $\mu$ M. The HAART dose was adjusted according to renal function. She was subsequently prescribed intermittent peritoneal dialysis in July 2003 and switched to continuous ambulatory peritoneal dialysis (CAPD) in August 2003.

Despite HAART (dose adjusted according to renal function: lamivudine 50 mg daily, stavudine 20 mg daily and nevirapine 200 mg twice daily), the CD4 lymphocyte count remained low (224 cells/ $\mu$ L). She developed CAPD-associated peritonitis 3 weeks after

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commencement of CAPD and developed septic shock attributed to multiple organisms, including extended-spectrum  $\beta$ -lactamase resistant *E. coli*, *Klebsiella* species, *Streptococcus milleri*, coliform organisms, *Candida glabrata* and *Candida tropicalis*. No evidence of bowel perforation was detected clinically. She received broad-spectrum antibiotics including vancomycin, piperacillin-tazobactam, amikacin and amphotericin B therapy to treat the peritonitis. The Tenckhoff catheter was removed. However, her condition deteriorated rapidly and she died 2 weeks after hospital admission.

## DISCUSSION

HIV-positive patients are at risk of developing ESRF attributed to HIV-associated nephropathy (HIVAN) and other types of glomerulonephritis [1]. HIV infection is endemic in Hong Kong. As of August 2003, the cumulative number of reported HIV cases in Hong Kong reached 2,116 [2]. Given the observed low incidence of HIVAN in the Asian HIV-infected population [3], it is not unexpected to find that the prevalence of HIV infection in the dialysis population in Hong Kong is extremely low. Our patient is one of the few cases ever prescribed peritoneal dialysis in Hong Kong.

The prevalence of HIV positivity in the dialysis population is much higher in the USA. According to the US Renal Data System (USRDS), the prevalence of HIV-positive dialysis patients is nearly 1% and is increasing by about 15% to 30% per year. This can probably be attributed to the large black population who are at an increased risk of developing HIVAN [4]. Although HAART slows the progression of HIVAN to ESRF in many patients [1], in light of the increasing prevalence of HIV infection in the USA, the total number of patients reaching ESRF is increasing [1].

Both CAPD and hemodialysis are effective modes of therapy for HIV-positive patients with ESRF. The prognosis for HIV-positive dialysis patients was dismal in the pre-HAART era. A substantial improvement in the prognosis has been observed since the introduction of HAART. In a retrospective study, patients on HAART had a significantly lower viral load compared to those on suboptimal antiretroviral therapy [5]. Four of seven hemodialysis patients on suboptimal antiretroviral therapy died after a mean follow-up period of  $13 \pm 10$  months, while only three of 15 patients on HAART died after a mean follow-up period of  $18 \pm 17$  months.

Despite encouraging reports, the morbidity and mortality of these patients remain high compared to age-matched patients with ESRF due to other causes [6]. In one study, the mean survival of HIV-positive

ESRF patients was around 15 months compared to 44 months in non-HIV infected patients [7]. In another series, the 1-year survival of HIV-positive dialysis patients was only 53% compared to 83% for their counterparts without HIV infection [8]. Vascular access complications including thrombosis and infection also occur more commonly in HIV-positive hemodialysis patients [1]. In general, a worse outcome is associated with increasing age at initiation of dialysis and low CD4 lymphocyte counts.

The main causes of death are infection and malnutrition. This may reflect the underutilization of HAART in this group of patients. In a retrospective survey, only 61% of HIV-positive dialysis patients received HAART [8]. Hypoalbuminemia is reported to be a strong predictor of mortality in ESRF patients [9]. In HIV-positive dialysis patients, the problem of malnutrition is particularly prominent. This may be related to the, in general, lower socioeconomic status of HIV-positive ESRF patients. A significantly higher degree of malnutrition at the time of entry and after the commencement of dialysis has been reported in a nationwide epidemiologic study performed in Italy [10].

Routine HIV testing in dialysis facilities remains controversial since it may be considered an infringement of civil liberties. The Centers for Disease Control and Prevention do not recommend routine screening of dialysis patients for HIV infection [1]. On the other hand, the potential advantages of identifying HIV-positive dialysis patients include better choice of dialysis modalities, preventive measures to avoid patient-to-patient transmission, early implementation of education and counseling programs to prevent transmission of the virus, use of antiretroviral therapy at an earlier stage of disease, and better treatment of opportunistic infections. It is worth noting that HIV testing employing enzyme immunoassay assays in dialysis patients is associated with a high false-positive rate. Confirmation with the Western blot technique is mandatory to make a definitive diagnosis [11].

It is prudent to emphasize that universal precautions must be practiced in all dialysis facilities regardless of the availability of HIV test results. In light of the rarity of nosocomial transmission in the dialysis setting [12], it is generally accepted that universally recommended precautions and simple maneuvers, such as thorough cleaning and disinfecting hemodialysis machines after use, are sufficient to prevent HIV transmission.

CAPD is an alternative therapy for HIV-positive patients reaching ESRF. Using the USRDS database, the survival of 5,229 HIV-positive hemodialysis patients was not different from that in 716 peritoneal dialysis patients [13]. Unlike hemodialysis, no vascular access is required and, thus, the potential risks of blood spills, patient-to-patient contamination, activation of white blood cells, and release of cytokines such as tu-

mor necrosis factor and interleukin-1 [14], and occupational exposure of hemodialysis personnel, were minimized [15].

Infectious complications are a major problem associated with CAPD. It has been reported that the HIV-positive CAPD population may develop peritonitis more frequently than other peritoneal dialysis patients [16]. An array of unusual organisms causing peritonitis has been reported, including *Pasturella multocida*, *Trichosporon beifellii* and *Mycobacterium avium* complex [17]. Owing to the underlying immunodeficiency in HIV-positive dialysis patients, as in our patient, polymicrobial peritonitis has been reported to be more common. However, in a retrospective analysis of 80 episodes of polymicrobial CAPD peritonitis in 432 patients, no difference in the polymicrobial peritonitis rate was observed between HIV-positive and HIV-negative patients [18].

Peritoneal dialysis effluent (PDE) from HIV-positive CAPD patients is potentially infectious. Viable and potentially infectious HIV virus has been isolated from PDE for up to 7 days in peritoneal dialysis bags at room temperature and for up to 48 hours in dry exchange tubing. Therefore, it would appear to be ethical to inform caregivers of the potential risk of infection. PDE should be discarded in a sink. A 30-minute exposure to 10% household bleach is an effective viricidal method to disinfect PDE for disposal [19–21]. Although no case of HIV transmission to caregivers of HIV-positive CAPD patients has been reported, personal protective equipment, including gloves, aprons and face shields, should be used while disposing of PDE [21].

Similar to the improvements in survival of HIV-positive patients with the use of HAART, survival of HIV-positive dialysis patients has also improved. There are three major classes of antiretrovirals: nucleoside analog reverse transcriptase inhibitors (NRTIs, e.g. zidovudine, didanosine, stavudine, lamivudine), non-nucleoside analog reverse transcriptase inhibitors (NNRTIs, e.g. nevirapine, efavirenz), and protease inhibitors (PIs, e.g. saquinavir, zidovudine, indinavir, nelfinavir). In HAART, a combination of either two NRTIs with a PI or two NRTIs plus one NNRTI is employed.

Most HIV medications are well tolerated even in the presence of renal dysfunction. NRTIs are primarily excreted by the kidneys. Dosage adjustment is advisable in patients with renal dysfunction to optimize drug exposure, reduce the risk of adverse drug effects and ensure cost-effectiveness in prescribing HAART [22]. A dose reduction of 50% to 70% for NRTIs may be required, and medications should be administered after dialysis. In a pharmacokinetic evaluation of lamivudine therapy in 11 HIV-positive dialysis patients (9 hemodialysis, 2 CAPD), lamivudine therapy at a dose of 25 mg/day was equivalent to a drug exposure

of 150 mg twice daily in those with normal renal function [23]. However, given the safety profile of high-dose lamivudine therapy, it is not unreasonable to prescribe lamivudine therapy at a dose higher than 25 mg/day in dialysis patients to prevent under-dosing. NNRTIs and PIs are primarily metabolized by the liver cytochrome P450 isoenzyme system, so dose adjustment is not usually required [21]. All patients on HAART should have their CD4 count and viral load monitored. Therapeutic drug monitoring is also available in some centers.

In conclusion, the decisions on whether to initiate dialytic therapy in HIV-positive ESRF should be individualized. CAPD is an effective dialytic therapy for HIV-positive patients, although infection remains the Achilles' heel. The potential risk of HIV transmission by PDE should be noted. An understanding of the pharmacokinetic properties of antiretroviral drugs in patients with renal dysfunction is mandatory to ensure safety and cost-effectiveness in prescribing HAART.

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